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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION III
841 Chestnut Building
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SUBJECT: Metcoa Radiation Site, Non-Radioactive Metals Cleanup Levels: Summary of Issues

DATE: 11-02-94

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TO: Jeff Dodd, OSC
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This memorandum follows up issues discussed in my memoranda of 3-22-94, 5-20-94, and 5-31-94.

The OSC tasked the toxicologist to review proposed cleanup levels and supporting documentation used to derive them for protectiveness at the Site. The results of this review were set forth in the 3-22-94 memorandum; this review identified several areas of concern with respect to inconsistencies with Superfund risk assessment process and possible errors.

The OSC then requested that the toxicologist derive cleanup levels that would take these issues into account. Those levels were presented in the 5-20-94 and 5-31-94 memoranda.

Upon reviewing EPA's proposed levels, certain Respondents objected on several counts. Objections raised on technical issues are summarized below:

1. <u>EPA assumed equal weighting of noncarcinogens with respect to total risk.</u>

This is a typical assumption used as a starting point because of its conservative nature. However, the Respondents were correct that chemicals could be divided into classes affecting similar target organs and a total Hazard Index of 1 be assigned to each category. Therefore, the EPA toxicologist divided the list of chemicals from the May memoranda into several categories by sensitive target organs: CENTRAL NERVOUS SYSTEM--manganese; KIDNEY--cadmium, molybdenum, chromium; GASTROINTESTINAL--copper; SKIN--arsenic, chromium; GROWTH/LONGEVITY (includes numbers based on LD50s and nonspecific effects such as shorter life span and decreased growth rate)--antimony, indium, nickel, and titanium.

The Respondents indicated a preference for using cadmium and

nickel as the chemicals that would be adjusted to achieve the target risk, rather than adjusting all chemical concentrations. This is acceptable to EPA since other chemicals at current concentrations pose a very minor contribution to the total risk. As long as existing risks are accounted for, cadmium and nickel can properly be considered to be the driving contaminants. Under those assumptions, non-radioactive soil contaminants other than cadmium and nickel would not warrant cleanup, but would be assumed to be present at the concentrations shown in the Respondents' supporting documentation.

Because the nickel and cadmium RfDs are not based on the same target organs, the approach taken by the Respondents was to derive a "renal RfD" for nickel. This renal RfD was then used to derive a "renal Hazard Quotient" for nickel that could be added to the Hazard Quotient for cadmium. (The Hazard Quotient for cadmium was already based on renal effects.) Pursuant to the conference call of 9-20-94, de maximis, inc., submitted a more detailed discussion of the derivation of the renal RfD for nickel.

The renal RfD derivation is innovative and was not employed in EPA's earlier memoranda. Upon receipt of the supporting material (10-24-94), EPA was able to assess the appropriateness of this value.

The renal RfD was derived from a NOAEL (No Observed Adverse Effects Level) based on a citation from ATSDR. ATSDR's Toxicological Profile for Nickel included the original source of this NOAEL of 25 mg/kg/day, which was a dog feeding study (Ambrose et al, 1976). Uncertainty factors of 10, 10, and 5 were applied to account for interspecies and intraspecies variability and use of a shorter-than-lifetime study. EPA finds use of the study to be acceptable. EPA finds the uncertainty factors to be appropriate; their application was in accordance with EPA guidance on the derivation of RfDs. The use of an uncertainty factor of 5 instead of 10 for the subchronic-to-chronic conversion was justified by the fact that the study was "long-term" (two years in dogs) but less than lifetime.

Therefore, EPA applies the renal RfD for nickel in determining cleanup levels for nickel that will be additive to those of cadmium, as set forth in the Respondents' supporting documentation.

2. The target cancer risk of 1E-6 proposed by EPA was too conservative.

The toxicologist had presented the OSC with a range of cleanup levels for carcinogens. The OSC has indicated that risks up to 1E-5 will be considered to be acceptable because

they are still within EPA's target risk range of 1E-4 to 1E-6. Existing on-site concentrations of carcinogens have been found to correspond to a cancer risk less than 1E-5.

3. The indium "error" identified by EPA was an error in the text, not the calculation; therefore, the provisional RfD for indium did not need to be changed.

This was found to be true and EPA estimations of indium risk dropped significantly, rendering indium no longer an important contributor to total site risk.

By 9-20-94, the above three issues had been resolved, and EPA could accept cleanup levels of existing concentrations for all metals except cadmium and nickel.

Two chemicals that could affect the cadmium and nickel cleanup levels in a minor way were chromium (renal group) and titanium (growth/longevity group). Two issues affecting these chemicals were raised by the Respondents during the conference call of 9-20-94:

4. Cleanup levels should be based on trivalent (less toxic) chromium rather than hexavalent chromium.

EPA usually assumes hexavalent chromium, in order to be conservative, in the absence of other evidence. However, the historical sampling data show a 95% UCL for hexavalent chromium in soil of less than 1 mg/kg. These data show that hexavalent chromium is expected to be a negligible contributor to on-site soil chromium; therefore, the use of trivalent chromium dose-response parameters is appropriate in determining clean-up levels at this Site.

5. Titanium should be dropped from the evaluation because of its nontoxic nature.

The Respondents had developed a provisional RfD of 1E-1 mg/kg/day for titanium, based on an oral mouse LD50 of titanium dioxide. EPA developed a provisional RfD of 6E-4 mg/kg/day, based on an intramuscular rodent dose of titanium. Because of the limited data available, there is no Agency-wide consensus on an RfD for titanium; therefore, best professional judgment must be used.

Titanium is a metal used in a large number of industrial applications. Titanium dioxide is a pigment that is also widely used; in fact, it is the most widely used titanium compound. At the outset, there is no clear and obvious indication of which number (provisional RfD of 1E-1 mg/kg/day or 6E-4 mg/kg/day) is more appropriate. However, sources in the literature were unanimous in emphasizing the relative nontoxicity of most titanium compounds (among them Lewis, 1992, and Doull, 1986). Use of the lower RfD (6E-4

mg/kg/day) would assume that titanium was more toxic than almost any other metal, which contradicts these sources. Also, for oral and dermal evaluation (which is appropriate for this site), a number based on oral rather than intramuscular application is probably more appropriate. For these reasons, the higher RfD of 1E-1, as used in Respondents' supporting documentation, seems more appropriate.

When the above factors (items 4 and 5) are taken into account, the contributions of chromium and titanium to total site risk decrease dramatically.

In order to determine the cadmium and nickel target concentrations, discrepancies between the Respondents' supporting documentation and the typical Superfund assessment were identified and examined. The use of a "renal RfD" for nickel has already been discussed, above. Three major differences relevant to dermal assessments were identified; each of these differences appeared in the dermal exposure pathway evaluation. As a preliminary matter, EPA supports the use of a skin surface area of 2000 $cm^2$ set forth in the Respondents' supporting documentation. The three differences and their effects on potential cleanup levels are discussed below.

6. The Respondents' documentation assumed a soil-to-skin adherence factor (AF) of 0.51 $mg/cm^2$. EPA Region III formerly used 1.45 $mg/cm^2$, based on potting soil, as per USEPA, 1989 (Risk Assessment Guidance for Superfund), as the acceptable soil-to-skin AF. EPA has modified the acceptable soil-to-skin AF downward to 1.0 $mg/cm^2$. This new number represents the upper end of the range recommended in the dermal guidance (USEPA, 1992). The acceptable range is 0.2 to 1.0 $mg/cm^2$, and 0.51 $mg/cm^2$ is within that range. Selection of the AF is generally a matter of professional judgment in the absence of site-specific studies. The use of an soil-to-skin AF of 0.51 $mg/cm^2$ would halve the dermal exposure as estimated by EPA. However, the overall effect on the target cleanup concentrations depends more upon other factors. The AF alone may have a negligible effect or an effect up to a factor of 2 on resulting cleanup levels.

7. Respondents' supporting documentation failed to indicate which method was used by the Respondents to adjust RfDs for absorbed dose. As noted in earlier memoranda, absorbed RfDs were given that were higher than intake RfDs. This is counterintuitive because it is impossible for a person to absorb a certain quantity of a substance greater than the overall intake of such substance. USEPA, 1989, Appendix A, describes the process for deriving absorbed RfDs from intake RfDs.

EPA's dermal assessment included arsenic, copper, manganese, and titanium. However, these four chemicals did not

contribute significantly to total risk, and cleanup levels were not derived for them. EPA adjusted all RfDs in the dermal assessment as per Integrated Risk Information System ("IRIS") or other guidance (See, Doull, 1986). In any case, the two chemicals for which this issue becomes significant are cadmium and nickel, whose adjusted doses are described here in detail.

The cadmium-in-food RfD (used to evaluate soil exposure, as opposed to the cadmium-in-water RfD) was adjusted by 2.5% for absorption as recommended on IRIS:

1E-3 mg/kg/day X .025 = 2.5E-5 mg/kg/day

Use of this number, instead of the unadjusted RfD used in the Respondents' supporting documentation, results in the cadmium dose at 1300 mg/kg exceeding a Hazard Quotient of 1. The use of the adjusted/absorbed RfD is appropriate when calculating a Hazard Quotient based on an absorbed dose, as specified in the guidance and as recommended by the source of the RfD.

Because EPA's original dermal assessment for nickel (5-20-94) was not based on the renal RfD, the following discussion summarizes derivation for a dermal RfD based on the Respondents' renal RfD. The Respondents' oral nickel RfD for renal effects was based on a dog feeding study. Therefore, EPA sought references on the oral absorption of nickel from food (in dogs, if possible). Unfortunately, the study on which the renal RfD was based (Ambrose et al, 1976) did not permit quantitation of the absorption, stating only that fecal excretion was "variable" and amounts retained in tissue were "small." The range of reviewed studies for oral absorption of nickel by rats and dogs is reported to be 1-10% (USEPA, 1986; ATSDR, 1993), with the lower end of the range representing absorption from food. Based on the fact that the nickel was given in food, and based on the recommendation of USEPA, 1989, for conservative estimates, it appears that 1% would be appropriate:

5E-2 mg/kg/day X .01 = 5E-4 mg/kg/day

Use of this number, instead of the adjusted-upward RfD as used in the Respondents' supporting documentation, decreases the amount of allowable nickel and therefore the target concentration. However, this has a minor effect in comparison with the next issue, the dermal absorption factor.

8. The dermal absorption factor (ABS) is probably the greatest difference and therefore has the most influence on the target cleanup concentrations. The ABS typically reflects the percentage of a chemical in a soil matrix that will be absorbed by the skin. The Respondents' supporting

documentation used a value of 0.001 (or 0.1%) for the dermal absorption of all metals from soil, including cadmium and nickel. This was expressed in risk assessment tables as (0.0001/hr) x 10 hr. The derivation of that expression was not clear.

EPA, in the original derivation of cleanup levels (5-20-94 and 5-31-94), used a dermal absorption factor of 1% for all metals from soil, including cadmium and nickel. With respect to cadmium, USEPA, 1992, set forth a range of dermal absorption factors of 0.1% to 1.0%. The 0.1% to 1.0% range for inorganics is also supported in Ryan et al, 1987. Region III, in keeping with the recommendation in USEPA, 1989, for conservative assumptions of the absorption factor, typically recommends the use of 1.0% for cadmium.

Studies specific to the absorption of nickel compounds have determined nickel absorption by non-occluded skin to be less than 0.1%, thus rendering 0.1%, as set forth in Respondents' supporting documentation, an acceptably conservative estimate for dermal absorption of this metal.

Therefore, the difference in a 1% or 0.1% ABS affects only cadmium and not nickel. In determining the cadmium cleanup concentration, the use of 1.0% as the appropriate dermal absorption factor for cadmium, rather than 0.1%, affects the resulting cadmium cleanup concentration by decreasing this cleanup concentration approximately seven-fold.

SUMMARY OF OUTSTANDING ISSUES

Based upon the above discussion, two issues remain outstanding: selection of the ABS for cadmium, and selection of the AF. EPA does not see any reason at this time to deviate from EPA-derived dose-response parameters for dermal absorption; the dermal RfDs in the MO/AR appear to have been erroneous. The selection of the cadmium ABS and the AF reflect ranges which require the use of professional judgment. To ensure protectiveness, EPA typically prefers to use 1) the best estimate of such parameters; or 2) the upper end of the probable range, where the best estimate is unknown. Possible cleanup levels for cadmium and nickel would depend upon these parameters and are shown in the table below.

| | ABS = 0.01 | ABS = 0.001 (MO/AR) |
|---|---|---|
| AF = 0.51 mg/cm² (MO/AR) | Cd = 130 mg/kg<br>Ni = 13000 mg/kg* | Cd = 700 mg/kg<br>Ni = 13000 mg/kg |
| AF = 1.0 mg/cm² | Cd = 70 mg/kg<br>Ni = 8000 mg/kg* | Cd = 500 mg/kg<br>Ni = 8000 mg/kg |

*ABS = 0.001 for nickel in all cases

The information in this memorandum is intended to follow up on issues identified in earlier memoranda, document changes in earlier recommendations and the reasons for those changes, and present the final issues remaining for consideration. This should enable the OSC to negotiate cleanup levels based on an informed decision.

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